REMARKS

I. Status Summary

Claims 8, 20, and 26-29 are pending in the present application and have been examined by the United States Patent and Trademark Office (hereinafter "the Patent Office") in a Non-Final Official Action dated June 17, 2009 (hereinafter the "Non-Final Official Action").

Claims 8, 20, and 26-28 have been rejected under 35 U.S.C. § 112, second paragraph, upon the contention that the claims are indefinite.

Claims 8, 20, and 26-29 have been rejected under 35 U.S.C. § 102(b) upon the contention that the claims are anticipated by U.S. Patent No. 5,683,894 to Edwards *et al.* (hereinafter referred to as "Edwards").

Claims 8, 20, and 26-29 have been rejected under 35 U.S.C. § 103(a) upon the contention that the claims are unpatentable over U.S. Patent No. 5,169,762 to Gray & Ullrich (hereinafter "Gray & Ullrich") and U.S. Patent No. 5,235,043 to Collins *et al.* (hereinafter "Collins").

Claims 8 and 29 have been amended to include that the claimed pharmaceutical preparations comprise a pharmaceutically acceptable carrier. No new matter has been added by the amendments to claims 8 and 29.

Reconsideration of the application as amended and based on the remarks set forth below is respectfully requested.

II. Response to the Rejection under § 112, Second Paragraph

Claims 8, 20, and 26-28 have been rejected under 35 U.S.C. § 112, second paragraph, upon the contention that the claims are indefinite. In support of this rejection, the Patent Office asserts that because pharmaceutical preparations/compositions must consist of at least two components, these preparation/composition claims are incomplete.

Applicants respectfully submit that if as asserted by the Patent Office, pharmaceutical preparations must consist of at least two components – one of which is a pharmaceutically acceptable carrier – then one of ordinary skill in the art would understand *a priori* that the pharmaceutical preparation comprising purified human

proNGF as the active ingredient of claims 1 and 29 would include a pharmaceutically acceptable carrier. As such, applicants respectfully submit that that it would not be necessary for claims 1 and 29 to explicitly recite the presence of a pharmaceutically acceptable carrier in claim 1 because one of ordinary skill in the art would understand that a pharmaceutical preparation comprising proNGF as the active ingredient would include a pharmaceutically acceptable carrier and thus would understand the metes and bounds of the pending claims.

However, in an effort to facilitate the instant prosecution and without acquiescing to the Patent Office's assertions, applicants have amended claims 1 and 29 to recite *inter alia* pharmaceutical preparations comprising a pharmaceutically acceptable carrier and purified human proNGF as the active ingredient. Support for this amendment can be found throughout the specification as filed in view of the understanding of one of ordinary skill in the art.

As a result applicants respectfully submit that the instant rejection of claims 8, 20, and 26-28 under 35 U.S.C. § 112, second paragraph, has been addressed, and respectfully request that it be withdrawn at this time. Allowance of these claims is also respectfully requested.

III. Response to the Rejection under § 102

Claims 8, 20, and 26-29 have been rejected under 35 U.S.C. § 102(b) upon the contention that the claims are anticipated by U.S. Patent No. 5,683,894 to Edwards *et al.* (hereinafter referred to as "Edwards").

After careful consideration of the rejection and the Patent Office's basis therefor, applicants respectfully traverse the rejection based on the remarks presented in its previous responses to the rejections under this section.

Particularly, applicants respectfully submit that Edwards discloses no preparations that would be properly considered a "pharmaceutical preparation" by one of ordinary skill in the art, and thus the Patent Office's refusal to consider the entire teachings of Edwards is believed to be improper under 35 U.S.C. § 102.

Furthermore, the Patent Office's assertion that the *in vitro* translated pro-NGF-beta solution taught in Example 2 of Edwards "would therefore reasonably be purified to

at least 90% purity based on this translation system" also fails to support the instant rejection. As has been pointed out by applicants previously, the product of an *in vitro* translation reaction includes numerous additional proteins that are necessary for performing the *in vitro* translation reaction. These proteins remain in the *in vitro* translation reaction product, and thus it is not believed to be possible for the Patent Office to assert that the amount of pro-NGF-beta produced on a mass basis or on any other basis exceeds the amount of other protein also present in the *in vitro* translation reaction by at least nine-fold in order to result in the pro-NGF-beta being "purified to at least 90% purity" as recited in claim 8.

Further, it might be that the Patent Office is asserting that the 90% element of claim 8 is inherently disclosed in Edwards since it is not explicitly disclosed. However, the ambiguity concerning how much total protein is present in the result of the *in vitro* translation reaction and what percentage of that total protein is pro-NGF-beta is believed to be fatal to the Patent Office's assertion since inherency "may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient". *See* M.P.E.P. § 2112, *citing In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999).

Summarily, applicants respectfully submit that the Patent Office has not presented a *prima facie* case of anticipation under 35 U.S.C. § 102(b) of claims 8, 20, and 26-29 over Edwards. Accordingly, applicants respectfully request that the instant rejection be withdrawn at this time. Allowance of these claims is also respectfully requested.

IV. Response to the Rejection under § 103

Claims 8, 20, and 26-29 have been rejected under 35 U.S.C. § 103(a) upon the contention that the claims are unpatentable over Gray & Ullrich and Collins. According to the Patent Office, Gray & Ullrich teach both the amino acid and nucleotide sequence of human proNGF, methods of making NGF proteins recombinantly using either prokaryotic or eukaryotic host cells, and pharmaceutical compositions thereof. The Patent Office concedes, however, that Gray & Ullrich are silent regarding the activity of proNGF as it relates to β-NGF. The Patent Office asserts, however, that the activity of

proNGF is directly related to its structure, and therefore, is an inherent property of proNGF.

After careful consideration of the rejection and the Patent Office's basis therefor, applicants respectfully traverse the rejection and submit the following remarks.

Initially, applicants respectfully traverse the Patent Office's assertion that the teachings of Edwards are not relevant to the instant rejection. Specifically, applicants respectfully submit that it is improper for the Patent Office to disregard Edwards' specific disclosure that pro-NGF is biologically inactive *per se*. Applicants respectfully submit that Edwards represents evidence of one of ordinary skill in the art's view that proNGF *per se* is biologically inactive.

To elaborate, it is axiomatic that the Patent Office must consider the prior art as a whole in determining the obviousness of claims, and particularly must consider art that teaches away from the claimed subject matter. It is improper for the Patent Office to exclude Edwards from the instant analysis merely because the instant rejection is based on Gray & Ullrich and Collins. Simply put, applicants respectfully submit that the instant rejection asserts that a pharmaceutical preparation that has purified human proNGF as the active ingredient as set forth in claims 8 and 29 is obvious over Gray & Ullrich and Collins. Given that Gray & Ullrich and Collins include no disclosure sufficient to suggest that purified human proNGF would have any activity *per se* (*i.e.*, could serve as an active ingredient as recited in the instant claims), the fact that Edwards explicitly discloses that pro-NGF has "little or no activity" is sufficient to teach away from the production of a pharmaceutical preparation that has purified human proNGF as the active ingredient. Therefore, applicants respectfully submit that as argued previously, Gray & Ullrich and Collins fail to support the instant rejection because they provide no teaching or suggestion that is sufficient to overcome Edwards' specific teaching.

Continuing, the Patent Office also asserts that "Gray et al teach both the amino acid and nucleotide sequence of human proNGF" and that "Collins clearly teach recombinant production of biologically active proteins, including proNGF, using expression in eukaryotic cells; and where in vitro production of biologically active polypeptides is routinely done in the art, as illustrated by the in vitro translation kits available from a number of companies". In supporting the instant rejection, the Patent

Office further relies on *KSR International Co. v. Teleflex Inc.* for the following proposition:

> the simple substitution of one known, equivalent element [i.e., proNGF for NGF] for another to obtain predictable results [i.e., increase DRG neuronal survival], or the combining of prior art elements [i.e., Collins' proneurotrophin polypeptides for the proNGF polypeptide] according to known methods [of making recombinant polypeptides] to yield predictable results [i.e., increase survival ofDRG neurons], reasonably supports a prima facie case of obviousness, especially given a finite number of predictable solutions [i.e., increased survival of DRG neurons using molecules that comprise the NGF amino acid sequence] where it would be obvious to try based on the teachings of Collins et al.

See Non-Final Official Action at pages 8-9.

Applicants respectfully submit that the Patent Office's reliance on *KSR* is unavailing in the context of the instant rejection. Applicants respectfully submit that the apparent assertion that proNGF is a "known, equivalent element" is clearly incorrect as it is only in the instant specification that proNGF is disclosed to have any activity at all. Thus, there is no disclosure in any reference cited by the Patent Office that would have led one of ordinary skill in the art to conclude that proNGF is an "equivalent" of NGF. Indeed, Edwards is believed to provide specific evidence to the contrary.

Additionally, *KSR* requires that the results obtained by the proposed substitution be "predictable". Here as well, applicants respectfully submit that there is no basis for the Patent Office to conclude that one of ordinary skill in the art would have believed "increased DRG neuronal survival" to have been a predictable activity of proNGF as of the filing date of the instant application. Applicants respectfully submit that Edwards specifically teaches and thus provides evidence against this conclusion, and it is only in applicants' own disclosure that the activity of proNGF *per se* is identified.

Thus, irrespective of what else Gray & Ullrich and Collins might teach, they provide no evidence that would have led one of ordinary skill in the art to believe that increased DRG neuronal survival was a predictable result of exposure to proNGF.

Summarily, applicants respectfully submit that Gray & Ullrich and Collins together do not support a *prima facie* case of obviousness of claims 8 and 29 because they provide no suggestion that a pharmaceutical preparation comprising purified human

proNGF as the active ingredient would have an activity *in vivo* analogous to β-NGF and promotes survival of dorsal root ganglia (DRG) sensory neurons (claim 8) and/or a biological activity in a dorsal root ganglion (DRG) assay that is about half that of human β-NGF in the same assay on a molar basis (claim 29). Claims 20 and 26-28 all depend from claim 8, and thus are also believed to have been distinguished over Gray & Ullrich and Collins. Applicants respectfully submit that claims 8, 20, and 26-29 are thus in condition for allowance. Applicants respectfully solicit a Notice of Allowance to that effect.

CONCLUSION

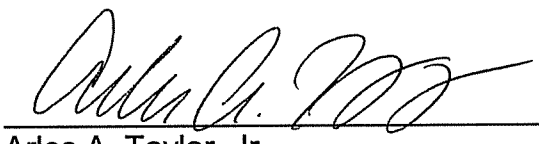
In light of the above amendments and remarks, it is respectfully submitted that the present application is now in proper condition for allowance, and an early notice to such effect is earnestly solicited.

If any small matter should remain outstanding after the Patent Examiner has had an opportunity to review the above Remarks, the Patent Examiner is respectfully requested to telephone the undersigned patent attorney in order to resolve these matters and avoid the issuance of another Official Action.

DEPOSIT ACCOUNT

The Commissioner is hereby authorized to charge any underpayment or credit any overpayment of fees associated with the filing of this correspondence to Deposit Account No. **50-0426**.

Respectfully submitted,
JENKINS, WILSON, TAYLOR & HUNT, P.A.

Date: October 7, 2009 By: 

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